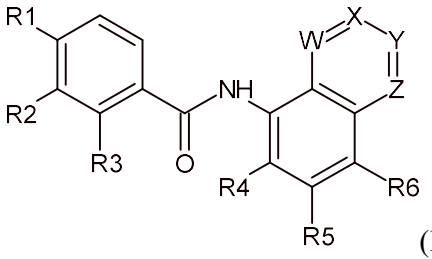
CLAIMS

1. A compound of formula (I) or any of its acceptable salts (I)

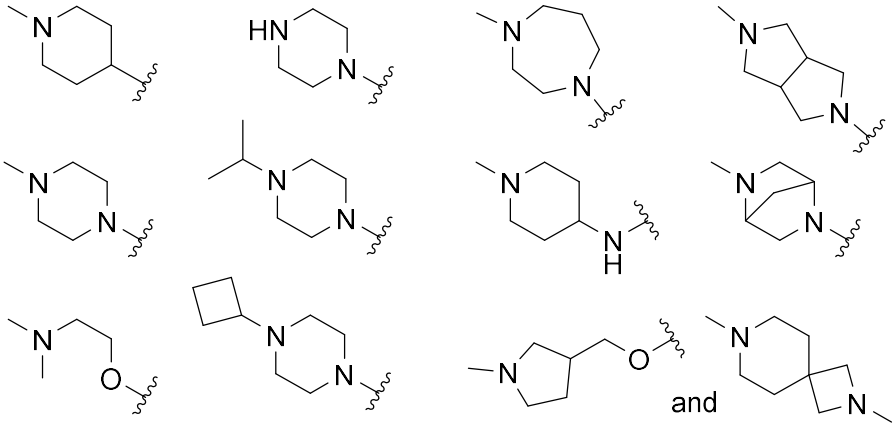


(I)

wherein

W, X, Y and Z each independently represents =CH- or -N=, provided that at most two of W, X, Y and Z both represent a -N= group,

R1 is selected from



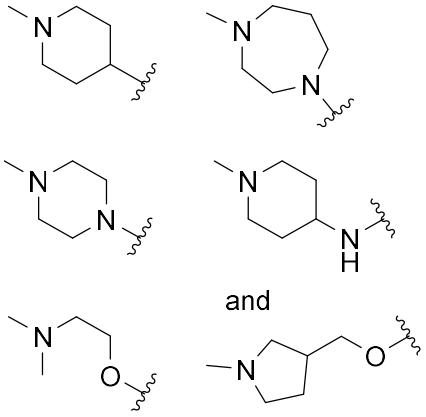
R2 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group, a -CO-(C_1-C_4)alkyl group, a -$CONH_2$ group, a SO_2-NH_2 group or a cyano group,

R3 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group, a cyano group, a (C_1-C_4)alkylsulfonyl group or a SO_2-NH_2 group, and

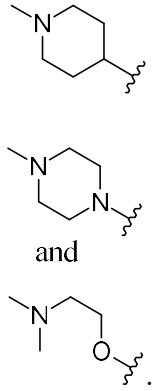
R4, R5 and R6 independently represent a hydrogen atom, a halogen atom, a -COOH group, a -COO(C_1-C_4)alkyl group, a (C_1-C_4)fluoroalkyl group, a (C_1-C_4)alkylsulfonyl group or a (C_1-C_4)alkoxy group.

2. The compound of formula (I) according to claim 1, wherein W is a -N= and X, Y and Z are =CH- or Y is a -N= and W, X and Z are =CH- or X is a -N= and W, Y and Z are =CH- or Z is a -N= and W, X and Y are =CH- or W and Z are -N= and X and Y are =CH- or X and Y are -N= and W and Z are =CH-.

3. The compound of formula (I) according to claim 1 or 2, wherein R1 is selected from



and more particularly selected from



.

4. The compound of formula (I) according to any one of claims 1 to 3, wherein R2 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group or a cyano group, and in particular a hydrogen atom, a fluorine atom, a methyl group, a methoxy group, a trifluoromethyl group or a cyano group.

5. The compound of formula (I) according to any one of claims 1 to 4, wherein R3 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a

(C_1-C_4)fluoroalkyl group or a (C_1-C_4)alkylsulfonyl group, and in particular a hydrogen atom, a fluorine or chlorine atom, a methyl group, a methoxy group, a trifluoromethyl group or a methylsulfonyl group.

6. The compound of formula (I) according to any one of claims 1 to 5, wherein R4, R5 and R6 independently represent a hydrogen atom, a halogen atom, a (C_1-C_4)fluoroalkyl group, a -COO(C_1-C_4)alkyl group, a (C_1-C_4)alkylsulfonyl group or a (C_1-C_4)alkoxy group, and in particular a hydrogen atom, a fluorine or chlorine atom, a trifluoromethyl group, a methyloxycarbonyl or a methoxy group.

7. The compound of formula (I) according to any one of claims 1 to 3, wherein

R2 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group, a -CO-(C_1-C_4)alkyl group or a cyano group, in particular a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group or a cyano group, more particularly a hydrogen atom, a fluorine atom, a methyl group, a methoxy group, a cyano group, a trifluoromethyl group,

R3 represents a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group, a cyano group or a (C_1-C_4)alkylsulfonyl group, in particular a hydrogen atom, a halogen atom, a (C_1-C_4)alkyl group, a (C_1-C_4)alkoxy group, a (C_1-C_4)fluoroalkyl group or a (C_1-C_4)alkylsulfonyl group, more particularly a hydrogen atom, a chlorine or fluorine atom, a methyl group, a methoxy group, a trifluoromethyl group or a methylsulfonyl group, and

R4, R5 and R6 independently represent a hydrogen atom, a halogen atom, a (C_1-C_4)fluoroalkyl group, a -COOH group, a -COO(C_1-C_4)alkyl group, a (C_1-C_4)alkylsulfonyl group or a (C_1-C_4)alkoxy group, in particular a hydrogen atom, a halogen atom, a (C_1-C_4)fluoroalkyl group or a (C_1-C_4)alkoxy group, more particularly a hydrogen atom, a chlorine or fluorine atom, a trifluoromethyl group, a methyloxycarbonyl group or a methoxy group.

8. The compound of formula (I) according to any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof, in particular hydrochloride salt thereof, characterized in that said compound is selected from the following compounds:

- (1) N-(5-fluoroquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (2) N-(8-fluoroisoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (3) N-(5-fluoroisoquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (4) N-(8-fluoroquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (5) N-(8-fluoroquinoxalin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (6) 4-(1-methylpiperidin-4-yl)-N-(quinolin-5-yl)benzamide,
- (7) N-(isoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (8) N-(isoquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (9) 4-(1-methylpiperidin-4-yl)-N-(quinolin-8-yl)benzamide,
- (10) 4-[2-(dimethylamino)ethoxy]-N-(isoquinolin-8-yl)benzamide,
- (11) 4-[2-(dimethylamino)ethoxy]-N-(quinolin-8-yl)benzamide,
- (12) 2-fluoro-4-(1-methylpiperidin-4-yl)-N-(quinolin-8-yl)benzamide,
- (13) 3-fluoro-N-(isoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (14) 4-(2-(dimethylamino)ethoxy)-N-(isoquinolin-5-yl)benzamide,
- (15) 4-(2-(dimethylamino)ethoxy)-N-(quinolin-5-yl)benzamide,
- (16) 2-methoxy-4-(1-methylpiperidin-4-yl)-N-(quinolin-8-yl)benzamide,
- (17) N-(isoquinolin-5-yl)-3-methoxy-4-(1-methylpiperidin-4-yl)benzamide,
- (18) 4-(1-methylpiperidin-4-yl)-N-(quinolin-8-yl)-2-(trifluoromethyl)benzamide,
- (19) 4-[2-(dimethylamino)ethoxy]-N-(phthalazin-5-yl)benzamide,
- (20) 4-(2-(dimethylamino)ethoxy)-N-(8-fluoroquinolin-5-yl)benzamide,
- (21) 3-cyano-N-(isoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (22) 4-(2-(dimethylamino)ethoxy)-N-(5-fluoroisoquinolin-8-yl)benzamide,
- (23) 4-(2-(dimethylamino)ethoxy)-N-(8-fluoroquinoxalin-5-yl)benzamide,
- (24) 3-fluoro-N-(isoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (25) N-(isoquinolin-5-yl)-2-methanesulfonyl-4-(1-methylpiperidin-4-yl)benzamide,
- (26) 4-[2-(dimethylamino)ethoxy]-N-(5-fluoroquinolin-8-yl)benzamide,

- (27) 4-(1-methylpiperidin-4-yl)-N-(quinolin-5-yl)-3-(trifluoromethyl)benzamide,
- (28) 4-(1-methylpiperidin-4-yl)-N-(quinoxalin-5-yl)benzamide,
- (29) 3-methyl-4-(4-methylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide,
- (30) N-(8-chloroquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (31) 4-[2-(dimethylamino)ethoxy]-N-(quinoxalin-5-yl)benzamide,
- (32) N-(8-chloroquinolin-5-yl)-4-[2-(dimethylamino)ethoxy]benzamide,
- (33) 4-[2-(dimethylamino)ethoxy]-N-(8-fluoroisoquinolin-5-yl)benzamide,
- (34) 4-[2-(dimethylamino)ethoxy]-N-(7-methoxyisoquinolin-5-yl)benzamide,
- (35) 4-(4-methylpiperazin-1-yl)-N-(quinolin-8-yl)benzamide,
- (36) 3-cyano-4-(2-(dimethylamino)ethoxy)-N-(isoquinolin-8-yl)benzamide,
- (37) N-(8-fluoroquinoxalin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (38) N-(isoquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (39) N-(isoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (40) 4-(4-methylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide,
- (41) 4-(4-methylpiperazin-1-yl)-N-(quinoxalin-5-yl)benzamide,
- (42) N-(5-fluoroquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (43) 4-(2-(dimethylamino)ethoxy)-3-methyl-N-(quinolin-8-yl)benzamide,
- (44) N-(8-fluoroquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (45) N-(isoquinolin-5-yl)-2-methyl-4-(4-methylpiperazin-1-yl)benzamide,
- (46) N-(8-chloroquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (47) 4-(2-(dimethylamino)ethoxy)-2-methyl-N-(quinolin-5-yl)benzamide,
- (48) 4-(2-(dimethylamino)ethoxy)-N-(isoquinolin-5-yl)-3-(trifluoromethyl)benzamide,
- (49) 4-(2-(dimethylamino)ethoxy)-N-(quinolin-5-yl)-2-(trifluoromethyl)benzamide,
- (50) 3-methoxy-4-(4-methylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide,
- (51) N-(8-chloroisoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide hydrochloride,

- (52) 4-(4-methylpiperazin-1-yl)-N-[5-(trifluoromethyl)isoquinolin-8-yl]benzamide hydrochloride,
- (53) 3-fluoro-N-(5-fluoroisoquinolin-8-yl)-4-{5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl}benzamide,
- (54) N-(8-methoxyisoquinolin-5-yl)-3-methyl-4-{7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}benzamide, and
- (55) 3-methyl-4-[(1-methylpyrrolidin-3-yl)methoxy]-N-(quinolin-8-yl)benzamide,
- (56) 2-fluoro-4-(4-methylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide,
- (57) 2-fluoro-N-(isoquinolin-8-yl)-4-[4-(propan-2-yl)piperazin-1-yl]benzamide,
- (58) N-(5-fluoroisoquinolin-8-yl)-3-methoxy-4-[(1R,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl]benzamide,
- (59 4-(4-cyclobutylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide,
- (60) N-(7-methoxyisoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (61) N-(5-chloroisoquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide hydrochloride,
- (62) N-(6-chloroisoquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (63) N-(6-methoxyisoquinolin-8-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (64) N-(8-chloroisoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (65) N-(8-methoxyisoquinolin-5-yl)-4-(1-methylpiperidin-4-yl)benzamide,
- (66) 4-(1-methylpiperidin-4-yl)-N-[5-(trifluoromethyl)isoquinolin-8-yl]benzamide,
- (67) 4-(1-methylpiperidin-4-yl)-N-(quinazolin-8-yl)benzamide,
- (68) 4-(4-methylpiperazin-1-yl)-N-(quinazolin-8-yl)benzamide,
- (69) N-(5-fluoroisoquinolin-8-yl)-4-(4-methyl-1,4-diazepan-1-yl)benzamide hydrochloride,
- (70) N-(8-methoxyisoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide hydrochloride,
- (71) N-(6-methoxyisoquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (72) 4-(1-methylpiperidin-4-yl)-N-(quinazolin-5-yl)benzamide,
- (73) N-(6-chloroisoquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,

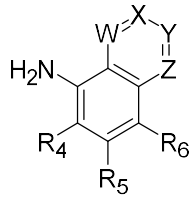
- (74) N-(8-chloroisoquinolin-5-yl)-3-methoxy-4-[(1-methylpiperidin-4-yl)amino]benzamide,
- (75) methyl 8-[4-(1-methylpiperidin-4-yl)benzamido]quinoline-5-carboxylate,
- (76) N-(5-fluoroisoquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (77) N-(5-chloroisoquinolin-8-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (78) 4-(1-methylpiperidin-4-yl)-N-(phthalazin-5-yl)benzamide,
- (79) N-(8-fluoroisoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide,
- (80) 4-(4-methylpiperazin-1-yl)-N-(quinazolin-5-yl)benzamide,
- (81) 4-(4-methylpiperazin-1-yl)-N-(phthalazin-5-yl)benzamide,
- (82) N-(7-methoxyisoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)benzamide hydrochloride,
- (83) 4-[2-(dimethylamino)ethoxy]-N-(quinazolin-5-yl)benzamide,
- (84) methyl 8-[4-(4-methylpiperazin-1-yl)benzamido]quinoline-5-carboxylate hydrochloride,
- (85) 4-[2-(dimethylamino)ethoxy]-N-(quinazolin-8-yl)benzamide,
- (86) N-(6-chloroisoquinolin-8-yl)-4-(2-(dimethylamino)ethoxy)benzamide,
- (87) 4-[2-(dimethylamino)ethoxy]-N-(6-methoxyisoquinolin-8-yl)benzamide,
- (88) N-(5-chloroisoquinolin-8-yl)-4-[2-(dimethylamino)ethoxy]benzamide,
- (89) 4-(2-(dimethylamino)ethoxy)-N-(7-methoxyisoquinolin-5-yl)benzamide hydrochloride,
- (90) 4-[2-(dimethylamino)ethoxy]-N-[5-(trifluoromethyl)isoquinolin-8-yl]benzamide hydrochloride,
- (91) methyl 8-{4-[2-(dimethylamino)ethoxy]benzamido}quinoline-5-carboxylate hydrochloride,
- (92) N-(8-chloroisoquinolin-5-yl)-4-[2-(dimethylamino)ethoxy]benzamide hydrochloride,
- (93) N-(isoquinolin-5-yl)-3-methyl-4-(1-methylpiperidin-4-yl)benzamide hydrochloride,
- (94) 2-methyl-4-(1-methylpiperidin-4-yl)-N-(quinolin-8-yl)benzamide hydrochloride,

- (95) 2-methyl-4-(4-methyl-1,4-diazepan-1-yl)-N-(quinolin-5-yl)benzamide,
- (96) 3-cyano-4-[(1-methylpyrrolidin-3-yl)methoxy]-N-(quinoxalin-5-yl)benzamide,
- (97) 4-(piperazin-1-yl)-N-(quinolin-8-yl)benzamide hydrochloride,
- (98) 4-[(1-methylpiperidin-4-yl)amino]-N-(quinolin-8-yl)-2-(trifluoromethyl)benzamide hydrochloride,
- (99) 4-(4-cyclobutylpiperazin-1-yl)-N-(isoquinolin-5-yl)-2-methoxybenzamide hydrochloride,
- (100) N-(isoquinolin-8-yl)-4-[4-(propan-2-yl)piperazin-1-yl]benzamide hydrochloride,
- (101) 2-fluoro-4-[(1R,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl]-N-(quinolin-8-yl)benzamide,
- (102) 4-[4-(propan-2-yl)piperazin-1-yl]-2-(trifluoromethyl)-N-[5-(trifluoromethyl)isoquinolin-8-yl]benzamide,
- (103) 4-[2-(dimethylamino)ethoxy]-3-fluoro-N-(quinolin-5-yl)benzamide,
- (104) N-(8-fluoroquinolin-5-yl)-2-methoxy-4-{7-methyl-2,7-diazaspiro[3.5]nonan-2-yl}benzamide hydrochloride,
- (105) 3-fluoro-N-(8-methoxyisoquinolin-5-yl)-4-(4-methyl-1,4-diazepan-1-yl)benzamide,
- (106) 4-[2-(dimethylamino)ethoxy]-2-fluoro-N-(quinolin-8-yl)benzamide,
- (107) 4-[2-(dimethylamino)ethoxy]-2-methoxy-N-(quinolin-5-yl)benzamide,
- (108) N-(8-fluoroquinolin-5-yl)-2-methanesulfonyl-4-{5-methyl-octahydropyrrolo[3,4-c]pyrrol-2-yl}benzamide,
- (109) N-(8-chloroisoquinolin-5-yl)-4-(4-cyclobutylpiperazin-1-yl)-3-fluorobenzamide hydrochloride,
- (110) 4-[2-(dimethylamino)ethoxy]-3-methoxy-N-(quinolin-8-yl)benzamide,
- (111) N-(isoquinolin-5-yl)-4-(4-methylpiperazin-1-yl)-2-(trifluoromethyl)benzamide,

- (112) N-(8-chloroquinolin-5-yl)-4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)benzamide,
- (113) 2-methanesulfonyl-4-(piperazin-1-yl)-N-(quinolin-5-yl)benzamide hydrochloride,
- (114) N-(isoquinolin-5-yl)-4-[(1-methylpiperidin-4-yl)amino]-3-(trifluoromethyl)benzamide,
- (115) 4-(4-methylpiperazin-1-yl)-2-(methylsulfonyl)-N-(quinolin-5-yl)benzamide,
- (116) 4-(4-methylpiperazin-1-yl)-N-(quinolin-8-yl)-3-(trifluoromethyl)benzamide,
- (117) N-(8-chloroisoquinolin-5-yl)-3-cyano-4-(4-cyclobutylpiperazin-1-yl)benzamide, and
- (118) 3-cyano-4-(4-methylpiperazin-1-yl)-N-(quinolin-5-yl)benzamide.

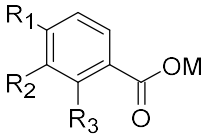
9. A process for preparing a compound of formula (I) as defined in any one of claims 1 to 8 or pharmaceutically acceptable salts thereof, comprising at least the following step:

- reacting a compound of formula (II):



(II)

wherein R4, R5, R6, W, X, Y and Z are as defined in any one of claims 1 to 7, with a compound of formula (VII):



(VII)

wherein R1, R2, R3 are as defined in any one of claims 1 to 7 and M represents an alkali metal or a hydrogen, in order to obtain a compound of formula (I),

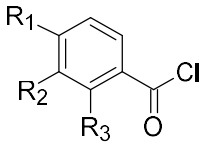
(i) by a peptide synthesis using a carboxyl activating agent, in particular N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide (EDCI) or N,N′-

Diisopropylcarbodiimide (DIC) with a racemization suppressor agent, in particular 1-Hydroxybenzotriazole (HOBt) or ethyl cyanohydroxyiminoacetate, and with an organic base in an aprotic polar solvent; or

(ii) first, by treating a compound of formula (VII) separately in presence of a chlorinating agent, in particular $SOCl_2$, and optionally an organic base in an aprotic solvent in order to form the corresponding acyl chloride derivative and then, by reacting said acyl chloride derivative with a compound of formula (II) by nucleophilic substitution using an organic base in an aprotic solvent.

10. Synthesis process for manufacturing a compound of formula (I) as defined in any one of claims 1 to 8 or anyone of its pharmaceutically acceptable salts, comprising at least the following step:

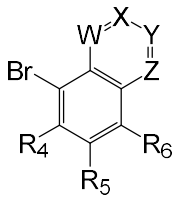
reacting a compound of formula (VIII),



(VIII),

wherein R2 and R3 are as defined in claim 1,

with a compound of formula (IX)



(IX)

wherein R4, R5, R6, W, X, Y and Z are as defined in claim 1,

via a first reaction with ammonia to convert the acyl chloride to a carboxamide, and second with a palladium-catalyzed Buchwald cross-coupling.

11. A pharmaceutical composition comprising at least one compound as defined in any one of claims 1 to 8 or anyone of its pharmaceutically acceptable salts, and also at least one pharmaceutically acceptable excipient.

12. A pharmaceutical composition comprising at least one compound as defined in any one of claims 1 to 8 or anyone of its pharmaceutically acceptable salts, an opioid, and

also at least one pharmaceutically acceptable excipient, wherein said opioid may be selected among alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dextropropoxyphene, dezocine,diampromide, diamorphone, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetylbuturate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene. ethylmorphine, etonitazene fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethideine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, remifentanyl, sufentonil, tapentadol, tilidine and tramadol, in particular among fentanyl, morphine, remifentanil and tramadol.

13. A compound according to any one of claims 1 to 8, alone or in combination with an opioid, in particular as defined in claim 12, for use as a medicament.

14. A compound according to any one of claims 1 to 8, alone or in combination with an opioid, in particular as defined in claim 12, for use in the prevention and/or treatment of pain.